

PATENT  
10/039,956  
Docket 091/009c

CLAIM AMENDMENTS

1. **CANCELLED**

2 to 15. **CANCELLED**

16. *(Currently amended)* A method of screening a substance, comprising:

a) obtaining a composition comprising undifferentiated hES cells proliferating on an extracellular matrix instead of feeder cells, in a medium conditioned by fibroblast feeder cells;

b) differentiating said hES cells;

a) c) contacting ~~a population~~ the population of differentiated cells with the substance;

b) d) determining any phenotypic or metabolic change in the cell that results from contact with the substance, and

e) e) correlating the change with cellular toxicity or modulation +

~~wherein the differentiated cells are obtainable by growing human embryonic stem (hES) cells on an extracellular matrix instead of feeder cells, but in a medium conditioned by fibroblast feeder cells, and then causing or permitting the hES cells to differentiate.~~

17 to 36. **CANCELLED**

37. *(Currently amended)* A method of screening a substance, comprising:

a) obtaining ~~a culture of a~~ a composition comprising undifferentiated pPS cells proliferating on an extracellular matrix instead of feeder cells, but in a medium conditioned by fibroblast feeder cells;

b) optionally causing or permitting the pPS cells to differentiate; then

c) combining the cells with the substance; and

d) determining any effect of the substance on the cells.

38. *(Previously presented)* The method of claim 37, wherein the extracellular matrix upon which the undifferentiated pPS cells are cultured is Matrigel® basement membrane matrix, laminin, or collagen.

39. *(Previously presented)* The method of claim 37, wherein the cells are undifferentiated when contacted with the substance.

40. *(Previously presented)* The method of claim 37, wherein the cells have been caused or permitted to differentiate before being contacted with the substance.

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41. *(Previously presented)* The method of claim 40, wherein the cells have been caused to differentiate by a process comprising replating them onto a surface that promotes differentiation.
42. *(Previously presented)* The method of claim 40, wherein the cells have been caused to differentiate by adding component(s) to the medium that promote differentiation towards a particular cell lineage.
43. *(Previously presented)* The method of claim 40, comprising causing the cells to differentiate into cells having characteristics of neuronal cells, glial cells, or neural precursors.
44. *(Previously presented)* The method of claim 40, comprising causing the cells to differentiate into cells having characteristics of hepatocytes.
45. *(Previously presented)* The method of claim 37, wherein the pPS cells are human embryonic stem (hES) cells.
46. *(Previously presented)* The method of claim 37, comprising determining the effect of the substance on growth of the cells.
47. *(Previously presented)* The method of claim 37, comprising determining whether the substance affects differentiation of the cells.
48. *(Previously presented)* The method of claim 37, comprising determining whether the substance affects expression of a marker or receptor by the cells.
49. *(Previously presented)* The method of claim 37, comprising determining whether the substance affects release of a marker or enzyme from the cells.
50. *(Previously presented)* The method of claim 37, comprising determining whether the substance affects DNA synthesis or repair in the cells.
51. *(Previously presented)* The method of claim 37, comprising analyzing the cells by metaphase spread.
52. *(Previously presented)* The method of claim 37, comprising determining whether the substance is toxic to the cells.

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53. *(Currently amended)* A method of screening a substance for its effect on undifferentiated human embryonic stem (hES) cells, comprising:
- a) obtaining ~~a culture of~~ a composition comprising undifferentiated pPS cells proliferating on an extracellular matrix instead of feeder cells, but in a medium conditioned by fibroblast feeder cells;
  - b) combining the undifferentiated hES cells with the substance; and
  - c) determining any effect of the substance on the cells.
54. *(Previously presented)* The method of claim 53, comprising determining the effect of the substance on growth of the cells.
55. *(Previously presented)* The method of claim 53, comprising determining whether the substance affects differentiation of the cells.
56. *(Previously presented)* The method of claim 53, comprising determining whether the substance affects expression of a marker or receptor by the cells.
57. *(Previously presented)* The method of claim 53, comprising determining whether the substance is toxic to the cells.
58. *(Previously presented)* The method of claim 16, comprising causing the cells to differentiate into cells having characteristics of neuronal cells, glial cells, or neural precursors.
59. *(Previously presented)* The method of claim 16, comprising causing the cells to differentiate into cells having characteristics of hepatocytes.
60. *(Previously presented)* The method of claim 16, comprising determining the effect of the substance on growth of the cells.
61. *(Previously presented)* The method of claim 16, comprising determining whether the compound affects expression of a marker or receptor by the cells.
62. *(Previously presented)* The method of claim 16, comprising determining whether the compound is toxic to the cells.
- 63 to 69. *CANCELLED*

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*Upon allowance of the application, please renumber the claims as follows:*

Claim	16	→	22
	37	→	1
	38	→	2
	39	→	3
	40	→	4
	41	→	5
	42	→	6
	43	→	7
	44	→	8
	45	→	9
	46	→	10
	47	→	11
	48	→	12
	49	→	13
	50	→	14
	51	→	15
	52	→	16
	53	→	17
	54	→	18

Claim	55	→	19
	56	→	20
	57	→	21
	58	→	23
	59	→	24
	60	→	25
	61	→	26
	62	→	27